AMENDMENTS TO THE CLAIMS

Applicants have amended claims 1-2, 4, 6-7, 13, 23-24, 26-27, 30, 33-34, 42, 44-45, and 47 without any intention of disclaiming equivalents thereof, and Applicants have cancelled claim 5 without prejudice to its subsequent reintroduction into this application or its introduction into a related application. The following list of claims replaces all prior versions and lists of claims in the application.

Listing of Claims:

1. (Currently Amended) A method for achieving high sensitivity detection and/or high accuracy quantitation of a plurality of target proteins in a biological sample, at least one of which comprises ~~the~~ an expression product of an alternative splicing form of a single DNA, the method comprising the steps of:

(1) fragmenting proteins in the sample using a predetermined denaturation and proteolytic protocol to generate a solution of polypeptide analytes comprising ~~recognition~~ sequences comprising peptide epitope tags (PETs) ~~displaying solvent-accessible binding surfaces~~ unambiguously indicative of the presence in the sample of the target proteins from which they are derived, at least one of which is unambiguously indicative of the presence in the sample of the alternative splicing form protein from which it is derived and comprises an amino acid sequence encoded by an RNA ~~comprising~~ spanning a splice junction;

(2) generating a plurality of capture agents specific for respective said PETs and immobilizing said capture agents to a solid support to provide ~~providing~~ an addressable array of plural capture agents~~, which capture agents selectively interact with a peptide epitope tag (PET) of said target proteins including a peptide epitope tag (PET) unambiguously indicative of the presence in the sample of said alternative splicing form protein~~;

(3) contacting said addressable array with said solution to ~~capture~~ yield captured polypeptide analytes bound by ~~binding~~ interaction between respective capture agents and said PETs presented by respective said polypeptide analytes; and,

(4) detecting the presence and amounts or absence of said target proteins in the sample, including at least said protein expression product of an alternative splicing form, by detecting the presence and amounts or absence of said captured polypeptide analytes, including said at least one polypeptide analyte comprising an amino acid sequence encoded by an RNA spanning a splice junction, using ~~with~~ secondary capture agents specific for sites separate from said PETs on the captured polypeptide analytes and labeled with a detectable moiety.

2. (Currently Amended) The method of claim 1 comprising providing an addressable array of capture agents comprising plural capture agents which selectively interact with different PETs from ~~the same target protein~~ one of said target proteins and quantitating, if present, the amount of the target protein in the sample by averaging ~~the~~ results obtained from each said capture agent.

3. (Previously Presented) The method of claim 1 wherein said capture agents comprise antibodies.

4. (Currently Amended) The method of claim 1, wherein said capture ~~agent~~ agents comprise a member selected from the group consisting of non-antibody polypeptide, PNA (peptide nucleic acids), scaffolded peptide, peptidomimetic compound, polynucleotide, carbohydrates, artificial polymers, plastibody, chimeric binding agent derived from low-affinity ligand, and small organic molecules.

5. (Canceled)

6. (Currently Amended) The method of claim 1, wherein a subset of said capture agents bind to ~~the same PET~~ one of said PETs.

7. (Currently Amended) The method of claim 1, wherein one of said target ~~protein~~ proteins has two or more different forms within said biological sample.

8. (Original) The method of claim 7, wherein said different forms include unprocessed / pro-form and processed / mature form.

9-12. (Canceled)

13. (Currently Amended) The method of claim 7, further comprising determining ~~the~~ a percentage of one form of the one of said target ~~protein~~ proteins as compared to ~~the~~ a total target protein, or ratio of a first form of the one of said target ~~protein~~ proteins to a second form of the one of said target ~~protein~~ proteins.

14-18. (Canceled)

19. (Original) The method of claim 1, wherein said sample is a body fluid selected from: saliva, mucous, sweat, whole blood, serum, urine, amniotic fluid, genital fluid, fecal material, marrow, plasma, spinal fluid, pericardial fluid, gastric fluid, abdominal fluid, peritoneal fluid, pleural fluid, synovial fluid, cyst fluid, cerebrospinal fluid, lung lavage fluid, lymphatic fluid, tears, prostatitc fluid, extraction from other body parts, or secretion from other glands; or from supernatant, whole cell lysate, or cell fraction obtained by lysis and fractionation of cellular material, extract or fraction of cells obtained directly from a biological entity or cells grown in an artificial environment.

20. (Previously Presented) The method of claim 1, wherein said sample is obtained from human, mouse, rat, frog, fish, fly, nematode, fission or budding yeast, or plant.

21. (Original) The method of claim 1, wherein said sample is produced by treatment of membrane bound proteins.

22. (Canceled)

23. (Currently Amended) The method of claim 1, wherein each of said secondary capture ~~agent~~ agents is labeled with a detectable moiety selected from: an enzyme, a fluorescent label, a stainable dye, a chemilumninescent compound, a colloidal particle, a radioactive isotope, a near-infrared dye, a DNA dendrimer, a water-soluble quantum dot, a latex bead, a selenium particle, or a europium nanoparticle.

24. (Currently Amended) The method of claim 23, wherein at least one of said secondary capture ~~agent~~ agents is labeled with a fluorophore.

25. (Canceled)

26. (Currently Amended) The method of claim 1, wherein said sample contains billion molar excess of unrelated proteins or fragments thereof relative to one of said target ~~protein~~ proteins.

27. (Currently Amended) The method of claim 1, wherein said ~~PET is~~ PETs are identified based on one or more ~~of the~~ protein sources selected from: sequenced genome or virtually translated proteome, virtually translated transcriptome, or mass spectrometry database of tryptic fragments.

28. (Previously Presented) The method of claim 1, wherein one or a combination of said target proteins serve as a biomarker.

29. (Canceled)

30. (Currently Amended) An array of capture agents for detecting and quantitating plural target splice variant proteins comprising the expression products of one or more splice variants of a single DNA within a biological sample, the array comprising a plurality of capture agents, each immobilized on a distinct addressable location on a solid support, plural of said capture agents specifically binding to recognition sequences comprising peptide epitope tags (PETs) displaying solvent accessible binding surfaces unambiguously indicative of the presence in the sample of the proteins from which they are derived, at least one of said PETs comprising an amino acid sequence encoded by an RNA ~~comprising~~ spanning a splice junction.

31. (Previously Presented) The array of claim 30, wherein said solid support comprises beads or an array device comprising features disposed in a manner that encodes the identity of said capture agents disposed thereon.

32. (Previously Presented) The array of claim 30, comprising 2 - 100 or more different capture agents.

33. (Currently Amended) The array of claim 30, wherein ~~a~~ one of said capture agents is a single chain antibody.

34. (Currently Amended) The array of claim 30, wherein ~~a~~ one of said capture ~~agent~~ agents is an antibody or antigen binding ~~portions~~ portion thereof.

35-41. (Canceled)

42. (Currently Amended) A method for detecting in a biological sample the presence or absence of plural target proteins, at least some of which comprise an expression product of one or more splice variants of a single DNA, the method comprising the steps of:

(1) fragmenting proteins in the sample, using a predetermined denaturation and proteolytic protocol, to generate a solution of polypeptide analytes comprising recognition sequences ~~displaying solvent accessible binding surfaces~~ unambiguously indicative of the presence in the sample of ~~splice variant~~ proteins from which they are derived, at least one of said recognition sequences comprising an amino acid sequence encoded by an RNA ~~comprising~~ spanning a splice junction;

~~(2) providing an addressable array of plural capture agents which selectively interact with binding surfaces of said polypeptide analytes;~~

~~(3)~~ (2) contacting said solution with an addressable array ~~and said solution~~ comprising a plurality of capture agents, each of which specifically binds a recognition sequence, and at least one of which specifically binds the at least one recognition sequence comprising an amino acid sequence encoded by an RNA spanning a splice junction, to ~~capture~~ yield captured polypeptide analytes bound by ~~binding~~ interaction between respective capture agents and said ~~binding surfaces~~ recognition sequences presented by respective said polypeptide analytes; and,

~~(4)~~ (3) detecting the presence or absence of said target ~~splice variant~~ proteins in the sample by detecting the presence or absence of said captured polypeptide analytes, including said polypeptide analyte comprising a recognition sequence comprising an amino acid sequence encoded by an RNA spanning a splice junction, using ~~with~~ secondary capture agents specific for available sites on respective said captured polypeptide analytes and labeled with a detectable moiety.

43. (Canceled)

44. (Currently Amended) The method of claim 42, wherein the addressable array of capture agents comprises plural capture agents which selectively interact with different ~~solvent accessible~~

~~binding surfaces~~ recognition sequences from the same target ~~splice variant proteins~~ protein in the sample.

45. (Currently Amended) The method of claim 44, further comprising quantitating, if present, the amount of ~~a~~ the target ~~splice variant~~ protein in the sample by averaging ~~the~~ results obtained from each said capture agent.

46. (Previously Presented) The method of claim 42, wherein said capture agents comprise antibodies.

47. (Currently Amended) The method of claim 6, wherein said subset of said capture agents have different affinity and/or avidity for ~~said same PET~~ the one of said PETs.